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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,763	05/11/2006	Piergiorgio Donati	277219US0PCT	8416

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EXAMINER	
GUCKER, STEPHEN	
ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
12/31/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/549,763	DONATI ET AL.	
	Examiner	Art Unit	
	STEPHEN GUCKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-10,12,15 and 18-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-10,12,15 and 18-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment

1. Due to Applicant's response filed 8/7/09, the 35 U.S.C. 112 second paragraph rejection has been withdrawn and the 35 U.S.C. rejection 102 under McNamara. The following 35 U.S.C. 102 and 103 rejections are maintained.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1, 5-10, 12, 18-24, and 26-29 are rejected under 35 U.S.C. 102(e) as being anticipated by US2006/0165733 ("Betz") for reasons of record and the following. Betz discloses a sterile liquid formulation in a storage container for pharmaceutical use (paragraphs [0009], [0016], [0061 – 0062], and [0074]) comprising hGH, sucrose stabilizer (at a concentration up to 30, 50, or 70 mg/ml; paragraph [0042]), 5-100 mM citrate buffer (paragraph [0040]), 0.05 – 4 mg/ml of poloxamer 188 (paragraph [0041]), 2 – 5 mg/ml phenol preservative (paragraph [0039]), at a pH of about 6.1 to about 6.3 (paragraph [0024]). PLURONIC® is the registered trademark for poloxamer, PLURONIC® F68 is the registered trademark for poloxamer 188.

Applicant's arguments filed 8/7/09 have been fully considered but they are not persuasive. Applicant argues that according to Lindemann Maschinenfabrik GMBH v. American Hoist and Derrick Co., 730 F.2d 1452, 1458 (Fed. Cir. 1984) and Ex parte Standish,

10 USPQ2d 1454, 1457 (Bd. Pat. App. & Int'f 1989), Betz does not anticipate the claims because Betz simply does not arrange the mere suggested components in the manner that is claimed. This is not convincing as Lindemann was drawn to a mechanical device that was not comprising of a list of components and could never anticipate the claimed invention in that case because:

> The '770 patent discloses an entirely different device, composed of parts distinct from those of the claimed invention, and operating in a different way to process different material differently. Thus there is presented here no possible question of anticipation by equivalents. See Tate Engineering, Inc. v. United States, 477 F.2d 1336, 1342, 193 Ct.Cl. 1088, 175 USPQ 115, 119 (Ct.Cl.1973). It is clear, moreover, that the device disclosed in the '770 patent, had it come after issuance of the '315 patent, could not be found an infringement of the asserted claims. The district court's analysis treated the claims as mere catalogs of separate parts, in disregard of the part-to-part relationships set forth in the claims and that give the claims their meaning.

The fact situation here is clearly different because there is no "disregard of the part-to-part relationships set forth in the claims" because the components disclosed in Betz have the same "part-to-part relationships" and perform the same function as the instant claims. Betz does not disclose an entirely different device; Betz does not disclose parts distinct from those of the claimed invention; and Betz does not disclose that these parts operate in a different way in relation to hGH. Therefore, Lindemann is not on point and is not analogous case law.

In much the same manner, neither is Standish on point with the instant fact pattern:

> Concerning these issues, the examiner acknowledges that appellant's claimed invention is not the same as (35 USC 102) patentee's *claimed* invention since Hanna's claim does not recite that the propellers rotate in opposite directions as required by the independent claims on appeal. However, it is the examiner's conclusion that the majority of the appealed claims are anticipated by patentee's *disclosed* invention. At odds with this conclusion is the examiner's finding that: Although the shading in the drawing Figs. of Hanna indicates that the spinner ears in one spinner are "extended in the opposite direction as the ears in the

> other spinner" as recited, whether this feature is shown is not entirely clear (Answer, page 4). **[2]** The examiner's finding of fact regarding Hanna's vagueness of this matter, with which we agree, controverts his conclusion of law regarding anticipation. This is because anticipation of a claimed product cannot be predicated on mere conjecture as to the characteristics of a prior art product. See *W.L. Gore and Associates, Inc. v. Garlock, Inc* ., 721 F.2d 1540, 220 USPQ 303, 314 (Fed.Cir. 1983). It follows that, even if Hanna is available as prior art against the claims on appeal, the above-noted §102(e) rejection cannot be sustained.

Again, Betz is not drawn to a mechanical device and it is not unclear what components Betz teaches to make Applicant's claimed invention – they are the same components that function in the same manner for the same purpose as Applicant's invention. It is clear that Betz discloses the same components to make the same composition, and no conjecture is required as to the characteristics of a prior art product comprising the same components as taught by the instant application.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a

later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 5-10, 12, 15, and 18-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Betz in view of US 5,567,677 (reference AA on IDS filed 9/19/05; "Castensson") for reasons of record and the following. The teachings of Betz are as set forth in **¶3** above. Betz does not teach the advantages of lowering the pH of a liquid formulation of hGH below 6.1. Castensson teaches that:

> "a large number of reactions can occur under different pH conditions and it is almost impossible to formulate a protein at a particular pH that eliminates all the modification reactions while maintaining high solubility and proper conformation of the protein. Until now a slightly alkaline pH has generally been used by manufacturers to avoid visible particles and to obtain a clear product. In most commercial products the pH is over 7, in spite of the higher risk for deamidation [of the hGH]. When Kabi Pharmacia's product Genotropin® [registered trademark for Kabi Pharmacia's hGH] is reconstituted, a pH of 6.7 is obtained at a hGH concentration of 16 IU/ml. This pH is a compromise between a pH giving a totally clear solution (pH 8) and pH 6 giving a lower deamidation rate but somewhat more opalescence." (column 2, lines 50-64)

Continuing on, Castensson discloses that:

> "Totally unexpected we have now found that solutions containing growth hormone in which citrate has been chosen as a buffer substance are more stable than those in which phosphate is the buffer." (column 3, lines 6-10)

Castensson teaches preferred liquid formulations of hGH with 2-40 mM citrate buffer at a pH of about 5.0 to 7.5 (column 3, lines 13-17). The liquid formulation of Castensson can contain carbohydrates (sucrose is a carbohydrate) and optionally a preservative (column 3, lines 23-28). McNamara teaches that chemical stability of liquid formulations of hGH are enhanced at a pH value of 6.0 or below (page 19, lines 9-10). Additionally, McNamara teaches that in the absence of PLURONIC® F68, aggregation and subsequent precipitation of hGH is maximal in the region of pH 5 to 6 (page 19, lines 21-22 and Figure 2) when the hGH liquid formulation is

agitated, and that in the absence of PLURONIC® F68, less than 1% of hGH remained in solution after agitation, but 0.1 – 0.5% PLURONIC® F68 even at pH 5.6 prevented virtually all of the hGH from aggregating and precipitating out of solution (page 19, line 26 to page 20, line 8 and Figure 3). It would have been obvious to one of ordinary skill in the art at the time of the invention to make a liquid formulation of hGH comprising citrate buffer as explicitly suggested by Castensson and to lower the pH value of said formulation to 6.0 or below as explicitly disclosed by McNamara as long as the formulation comprised at least 0.1 – 0.5% PLURONIC® F68 to prevent the hGH from aggregating and precipitating out of solution, making it worthless as a pharmaceutical if agitated. Because the combination of the prior art references teach that citrate buffer and a pH at or below 6.0 in the presence, but not absence, of PLURONIC® F68 greatly improves the beneficial and desirable stability of liquid hGH formulations so that it is not ruined as a pharmaceutical composition upon agitation, the instant invention is rendered *prima facie* obvious.

Applicant's arguments filed 8/7/09 have been fully considered but they are not persuasive because Applicant argues "the skilled person would be led away from using sucrose and even more so from combining it with citrate buffer for which there is no experimental basis." The Examiner respectfully disagrees with Applicant's argument because, as the rejection of record explained, "the liquid formulation of Castensson can contain carbohydrates (sucrose is a carbohydrate)." Applicant's other arguments concerning the deficiencies of Betz were discussed in detail above. As far as hindsight reconstruction, the Examiner reminds Applicant because of the finite number of choices taught by the prior art to produce the same liquid formulation of hGH as the instant invention, the substitution of one

component to perform the same function as another component is obvious. Essentially, all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention because the nexus between the references makes the substitution of a known functionally similar component from a finite list for a known similar in order to produce a known similar result with a reasonable expectation of success is prima facie obvious. See KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727 (U.S. 2007).

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is 571-272-0883. The examiner can normally be reached on Mondays through Fridays from 0930 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. G./
Examiner, Art Unit 1649
Stephen Gucker
December 29, 2009

/Jeffrey Stucker/
Supervisory Patent Examiner, Art Unit 1649